

We Claim:

1. A non-cytolytic recombinant human immunodeficiency virus-1 (HIV-1) wherein the natural signal sequence (NSS) of the virus' envelope glycoprotein is replaced with an essentially non-cytolytic signal sequence.
- 5 2. A non-cytolytic recombinant HIV-1 wherein the natural signal sequence (NSS) of the virus' envelope glycoprotein is modified to provide an essentially non-cytolytic signal sequence.
- 10 3. A non-cytolytic recombinant retrovirus according to claim 2 wherein the modified essentially non-cytolytic signal sequence is modified to contain no more than one positively charged amino acid.
4. A non-cytolytic recombinant retrovirus according to claim 3 wherein the modified essentially non-cytolytic signal sequence is modified to contain zero positively charged amino acids.
- 15 5. A retrovirus according to claim 1 wherein the NSS is replaced with mellitin signal sequence (MSS) or IL-3 signal sequence (ILSS).
6. A retrovirus according to any one of claims 1-5 wherein the retrovirus is rendered avirulent.
7. A retrovirus according to claim 6 wherein the retrovirus is rendered avirulent by deletion of the *nef* gene.
- 20 8. A vaccine incorporating the retrovirus of any one of claims 1 to 7.
9. ✓ A method of preventing or treating a retroviral infection comprising administering to an animal in need thereof, an effective amount of an essentially non-cytolytic recombinant HIV-1 wherein the NSS of the virus' envelope glycoprotein is replaced with an essentially non-cytolytic NSS and the retrovirus is rendered avirulent.
- 25 10. ✓ A method of preventing or treating a retroviral infection comprising administering to an animal in need thereof, an effective amount of an essentially non-cytolytic recombinant HIV-1 wherein the NSS of the virus envelope glycoprotein is

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modified to provide a non-cytolytic NSS.

11. The method of claim 10 where the modification to provide a non-cytolytic NSS results in no more than one positively charged amino acid in the NSS sequence.

5 12. The method of claim 11 where the modification to provide a non-cytolytic NSS results in zero positively charged amino acids.

13. A method according to claim 9 wherein the non-cytolytic signal sequence is selected from the group consisting of the mellitin sequence and the IL-3 signal sequence.

10 14. A method according to any one of claims 9-13 wherein the virus is rendered avirulent by deletion of the *nef* gene.

15. A vaccine comprising an essentially non-cytolytic recombinant HIV-1 wherein the NSS of the virus envelope glycoprotein is replaced with an essentially non-cytolytic NSS.

15 16. A vaccine comprising an essentially non-cytolytic recombinant HIV-1 wherein the NSS of the retrovirus envelope glycoprotein is modified to provide an essentially non-cytolytic NSS and the retrovirus is rendered avirulent.

17. A vaccine according to claim 16 wherein the natural signal sequence is modified to reduce the number of positive amino acids to no more than one positive amino acids.
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18. A vaccine according to claim 17 wherein the number of positive amino acids is zero.

19. A vaccine according to claim 15 wherein the essentially non-cytolytic signal sequence is selected from the group consisting of the mellitin sequence and the IL-3 signal sequence.
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20. A vaccine according to any one of claims 15 to 19 wherein the virus is rendered avirulent by deletion of the *nef* gene.

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21. A vaccine according to anyone of claims 15 to 20 further comprising an adjuvant.

22. ✓ A method of killing a target cell comprising administering an effective amount of a recombinant virus containing NSS of HIV-1 and a recognition site specific
5 to the target cell, to the cell.

23. A method according to claim 22 wherein the NSS of HIV-1 is of HIV-1 envelope glycoprotein.

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24. A method according to claim 22 or 23 wherein the recombinant virus is VSV.

10 25. A method according to any one of claims 22, 23 or 24 wherein the cell is in an animal.

26. A method of preventing apoptosis induced by the NSS of HIV-1 protein comprising administering an effective amount of antagonist to the HIV-1 NSS protein to an animal in need thereof.

15 27. A method according to claim 26 wherein the protein is an HIV-1 NSS envelope glycoprotein.

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28. A method according to claim 26 or 27 wherein the antagonist is an antibody to NSS.

20 29. A method of inhibiting the effects of the NSS of HIV-1 comprising administering an effective amount of an antisense oligonucleotide that is complementary to a nucleic acid sequence for an NSS protein gene, to an animal in need thereof.

30. A method according to claim 29 wherein the protein is an HIV-1 NSS envelope glycoprotein.